

M 1905.00

- 25 -

Claims:

1. A combined ^{Preparation} presentation for simultaneous, separate or sequential use as an ultrasound contrast agent, said preparation comprising:
- 5 i) an injectable aqueous gas dispersion; and
- ii) a separately administrable substance or substances capable of destabilising said dispersed gas so as at least transiently to increase the size thereof.
- 10 2. A combined preparation as claimed in claim 1 wherein the dispersed gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, an optionally halogenated silane, an optionally halogenated low molecular weight hydrocarbon, a ketone, an ester or a mixture of any of the foregoing.
- 15 3. A combined preparation as claimed in claim 2 wherein the dispersed gas comprises sulphur hexafluoride or a perfluorocarbon.
- 20 4. A combined preparation as claimed in claim 3 wherein said perfluorocarbon is perfluoropropane, perfluorobutane or perfluoropentane.
- 25 5. A combined preparation as claimed in ~~any of the preceding claims~~ wherein the dispersed gas is stabilised by an initially coalescence-resisting/surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.
- 30 6. A combined preparation as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.
- 35

7. A combined preparation as claimed in claim 6 wherein at least 75% of said surfactant comprises phospholipid molecules individually bearing net overall charge.

5

8. A combined preparation as claimed in claim 7 wherein said charged phospholipid molecules are selected from phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid and cardiolipin molecules.

10

10. A combined preparation as claimed in any of the preceding claims comprising one or more destabilising substances which induce growth of the dispersed gas by flocculation, aggregation, agglomeration, coalescence, fusion or Ostwald ripening.

15

11. A combined preparation as claimed in claim 10 comprising one or more destabilising substances selected from inorganic salts, aliphatic alcohols, aliphatic aldehydes, aliphatic ketones, aliphatic esters, aliphatic ethers, aliphatic amides, aliphatic nitriles, carbohydrates, polyethers, polysaccharides, polyaminoacids, polyvinylpyrrolidone, fatty alcohols, fatty acids, fatty amines, surfactants, steroids, acids, bases and hydrotropes.

20

25

12. A combined preparation as claimed in claim 11 comprising one or more destabilising substances selected from calcium chloride, magnesium chloride, ethanol, isopropanol, ethylene glycol, propylene glycol, glycerol, sorbitol, acetaldehyde, acetone, methyl formate, methyl acetate, propyl formate, ethyl acetate, ethyl methyl ether, methyl propyl ether, di-isopropyl ether, N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile, glucose, sucrose, polyethylene glycol, polypropylene glycol, polyoxyethylene-polyoxypropylene

30

35

5

10

15

~~1 to 12~~ which further includes a therapeutic drug.

20

25

system of said subject;

30

35

18. A method as claimed in claim 17 wherein

destabilising substance is administered subcutaneously, intramuscularly, intravenously or by inhalation.

19. A method as claimed in claim 17 ~~or claim 18~~ wherein
5 a vasodilator drug is coadministered to the subject.

20. A method as claimed in claim 19 wherein said vasodilator drug is adenosine.

10 21. Use of a contrast agent as claimed in ^{claim} ~~any of claims 1 to 12~~ in ultrasound therapy.

22. Use as claimed in claim 21 wherein said therapy
15 involves cell killing or blocking of blood flow to a site of interest.

USE
CLAIMS

add C17

00321 897 4300